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New glucosyltransferase inhibitors - are extracted from fermented tea leaves and used for the prevention of dental caries
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Patent Family

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CA 2039538	A	19911001				199151	
AU 645069	B	19940106	AU 9173944	A	19910402	199408	
US 5409692	A	19950425	US 91677335	A	19910329	199522	
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JP 95063294	B2	19950712	JP 90301200	A	19901108	199532	
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DE 69111652	E	19950907	DE 611652	A	19910402	199541	
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Abstract:
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A glucosyltransferase (GT) inhibitor is claimed comprising as an active ingredient an extract of fermented tea leaves. Also claimed is a GT inhibitor comprising as an active ingredient a non-adsorbed fraction of an extract of fermented tea leaves, the non-adsorbed fraction having been obtd. by subjecting the extract to adsorption treatment using a synthetic adsorbent and being other than extract fractions adsorbed on the synthetic adsorbent. Pref. the non-absorbed fraction of the extract has catechins and caffeine eliminated by the adsorption treatment. The extract is pref. obtd. using an aqs. soln. contg. 0-90 vol% EtOH.

USE/ADVANTAGE - The GT inhibitor can be used in e.g. toothpaste, food or beverages for the prevention of dental caries. The non-adsorbed fraction has strong GT inhibitory activity without a characteristic taste or smell. (21pp Dwg.No.0/0)

EP 449332 B

A glucosyltransferase inhibitor comprising as an active ingredient a non-adsorbed fraction of an extract of fermented tea leaves, said non-adsorbed fraction having been obtained by subjecting the extract to adsorption treatment while using a synthetic adsorbent selected from adsorbents produced by polymerisation of styrene and divinylbenzene or by polymerisation of methacrylic acid and said non-adsorbed fraction being other than extract fractions adsorbed on the synthetic adsorbent.

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US 5409692 A

A glucosyltransferase (GT) inhibitor is claimed comprising as an active ingredient an extract of fermented tea leaves. Also claimed is a GT inhibitor comprising as an active ingredient a non-adsorbed fraction of an extract of fermented tea leaves, the non-adsorbed fraction having been obtd. by subjecting the extract to adsorption treatment using a synthetic adsorbent and being other than extract fractions adsorbed on the synthetic adsorbent. Pref. the non-absorbed fraction of the extract has catechins and caffeine eliminated by the adsorption treatment. The extract is pref. obtd. using an aq. soln. contg. 0-90 vol% EtOH.

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(54) Glucosyltransferase inhibitors, as well as dental caries prevention methods and anticarious foods using the same.

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PATENT ABSTRACTS OF JAPAN vol. 14, no. 176 (C-707)(4119), 9 April 1990; & JP - A - 225413 (ITOUEN K.K.) 26.01.1990

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PATENT ABSTRACTS OF JAPAN vol. 13, no. 182 (C-591)(3530), 27 April 1989; & JP - A - 19922 (TAIYO KAGAKU CO. LTD.) 13.01.1989

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Description

BACKGROUND OF THE INVENTION

1) Field of the Invention

The present invention relates to glucosyltransferase inhibitors and methods for preventing dental caries by using the same, and more specifically to glucosyltransferase inhibitors comprising as an active ingredient an extract from fermented tea leaves having glucosyltransferase inhibitory action, methods for preventing dental caries by using the same and anticarious beverages and foods containing the same.

2) Description of the Related Art

Although a variety of theories were proposed in the past as to a possible cause for dental caries, it is now recognized that dental caries is a type of bacterial infectious disease based on the chemicoparasitic theory proposed by Miller.

The mechanism of occurrence of dental caries on the basis of the above theory is as follows. Namely, an enzyme called "glucosyltransferase", which is produced by oral streptococci, notably by *Streptococcus mutans* produces a sticky, insoluble polysaccharide (glucan) by using as a substrate sugar in the mouth. Cells of *Streptococcus mutans* (hereinafter abbreviated as "*S. mutans*") adhere to the surfaces of teeth by the glucan so produced, so that they form granules (dental plaques). Various microorganisms led by *S. mutans* are symbiotically growing in the dental plaques. Organic acids are produced by the metabolic activities of these microorganisms. The pH on the surfaces of the teeth drops as a result of the action of these organic acids, resulting in decalcification of the enamel surfaces. Consequently, dental caries takes place and proceeds.

Further, the formation of dental plaques is also believed to cause paradental diseases and bad breath in addition to dental caries.

Based on the findings described above, various investigations have been conducted with a view toward developing, as preventive measures for dental caries, antibacterial agents for oral microorganisms, inhibitors for glucosyltransferase, and enzymes capable of decomposing polysaccharides which glucosyltransferase forms using sugar as a substrate. However, no anticarious method having satisfactory effects has yet been found.

Prevention of dental plaque formation by suppressing pressing the activities of glucosyltransferase is considered likely to become an effective means for the prevention of occurrence of dental caries especially in view of the fact that dental plaque formed by oral streptococci led by *S. mutans* acts as a cause for dental caries. To date, however, no practically usable glucosyltransferase activity inhibition substance has yet been found.

It is known from Chemical Abstracts, Vol. 104, No. 15 that among tea components gelatin-precipitable tannins, and (+)-catechin have glucosyltransferase inhibiting activity.

It has further been known that extracts obtained by the extraction of tea leaves may be used as a component of tooth pastes effective against karies (Patent Abstracts of Japan, Vol. 13, No. 182, C-591, 3530).

The present inventors have carried out an extensive investigation with a view toward finding a substance which can effectively inhibit glucosyltransferase but has no adverse effects on the human body. As a result, it has been revealed that a substance capable of extremely effectively inhibiting the activities of glucosyltransferase produced by *S. mutans* is contained in an extract of fermented tea leaves and this substance is not adsorbed even by synthetic adsorbents, leading to the completion of the present invention.

An object of the present invention is to provide a glucosyltransferase inhibitor which comprises as an active ingredient a non-adsorbed fraction of an extract of fermented tea leaves. The non-adsorbed fraction has been obtained by subjecting the extract to adsorption treatment while using a synthetic adsorbent and is other than extract fractions adsorbed on the synthetic adsorbent.

A further object of the present invention is to provide a food or beverage for the prevention of dental caries. The food or beverage comprises an effective amount of the above inhibitor.

A still further object of the present invention is to provide for the prevention of dental caries, which comprises taking a food or beverage containing an effective amount of the glucosyltransferase inhibitor.

According to the present invention there is provided a glucosyltransferase inhibitor comprising as an active ingredient a non-adsorbed fraction of an extract of fermented tea leaves, said non-adsorbed fraction having been obtained by subjecting the extract to adsorption treatment while using a synthetic adsorbent

selected from adsorbents produced by polymerisation of styrene and divinylbenzene or by polymerisation of methacrylic acid and said non-adsorbed being other than extract fractions adsorbed on the synthetic adsorbent.

In a further aspect of the present invention, there is also provided a food or beverage for the prevention of dental caries, which comprises an effective amount of one of the above inhibitors.

In a still further aspect of the present invention, there is also provided for the prevention of dental caries, which comprises taking a food or beverage containing an effective amount of one of the above inhibitors.

In a still further aspect of the present invention, there is also provided use of a non-adsorbed fraction of an extract of fermented tea leaves for the production of a glucosyltransferase inhibitor.

Catechins have already been known to have proliferation inhibitory action against *S. mutans*. Their activity is however extremely weak so that a practical level of anticarious activity cannot be expected at concentrations actually usable in respect of taste and flavor.

In view of the fact that, as will be demonstrated in the subsequent example, excellent glucosyltransferase inhibition activity is also found on the non-adsorbed fraction which does not contain catechins and caffeine at all or contain them in extremely small amounts, it is evident that the effects of the present invention are not related to catechins.

The glucosyltransferase inhibitor of the present invention can therefore be used as a new way for the prevention of dental caries, which makes use of the glucosyltransferase inhibitory activity.

In particular, use of the non-adsorbed fraction as an active ingredient makes it possible to add the same at desired concentrations to various beverages, drinks and foods because this fraction has strong glucosyltransferase inhibitory activity and moreover does not have a characteristic taste or smell. It is therefore possible to produce beverages, drinks and foods having extremely good anticarious activity.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

The active ingredient of the glucosyltransferase inhibitor according to the present invention is present in an extract of fermented tea leaves. Described specifically, it is contained in a fraction not adsorbed on a synthetic adsorbent when the extract is treated with the synthetic adsorbent. The above fraction may hereinafter be called a "non-adsorbed fraction".

The non-adsorbed fraction contains no catechins and caffeine, representative components of tea, or contains them only in extremely small amounts.

In the production of the glucosyltransferase inhibitor of the present invention, Oolong tea leaves, black tea leaves, Pu-erh tea leaves and the like are all usable as fermented tea leaves to be employed as a raw material for extraction.

Examples of the solvent usable for the extraction include water alone and desired mixtures of water and one or more polar solvents such as lower alcohols, e.g., methanol and ethanol, and acetone. Since efficient extraction of the active ingredient of the present invention is not feasible if a polar solvent is used alone, the polar solvent must be used in the form of a mixture with water, with their preferred mixing ratio being such that the solvent amounts to 90 wt.% or less. Among these solvents, it is preferable to use water, ethanol or a mixture thereof from the standpoint of safety in view of the fact that the extract and the like are eventually incorporated in oral preparations or foods.

Although no particular limitation is imposed on the ratio of fermented tea leaves to the solvent upon extraction, it is preferable to use the solvent in an amount 2-1,000 times by weight, especially 20-100 times by weight the amount of the fermented tea leaves in view of the extracting operation and efficiency.

The extraction temperature can conveniently be set within the range of from room temperature to the boiling point of the solvent under normal pressure. The extraction time can preferably range from 10 minutes to 24 hours although it varies depending on the temperature of the extraction.

To obtain a non-adsorbed fraction from the above-obtained extract of the fermented tea leaves, it is necessary to treat the extract with a synthetic adsorbent, as specified in claim 1.

Synthetic adsorbents employed for the fractionation of the extract of the fermented tea leaves are aromatic synthetic adsorbents produced by polymerization of styrene and divinylbenzene and methacrylic synthetic adsorbents produced by polymerization of methacrylic acid. A typical commercial product of aromatic synthetic adsorbent is "DIAION HP21" (trade name, products of Mitsubishi Kasei Corp., Tokyo, Japan).

The synthetic adsorbent treatment can be effected preferably by packing a column with the adsorbent, charging the extract of the fermented tea leaves into the column and then washing the resin with water.

Upon treatment of the extract of the fermented tea leaves with such a synthetic adsorbent, it is preferable to subject the extract to pretreatment in order to achieve complete fractionation. The pretreatment may comprise removal of any organic solvent from the extract, for example, by concentration of the extract under reduced pressure, followed by full dilution of the resultant concentrate with water.

The extract of the fermented tea leaves and the non-adsorbed fraction, both obtained in the above-described manner, can be used in any form - for example, as they are, in other words, directly after the extraction and the synthetic adsorbent treatment; as concentrates; or as dried products obtained by removing the solvent from the extract and the non-adsorbed eluate fraction. It is however preferable to use them in a dried form from the standpoints of storability and safety, i.e., the complete elimination of the organic solvent.

The glucosyltransferase inhibitor of the present invention is formulated into a preparation by mixing the above extract or non-adsorbed fraction with various components which have conventionally been used.

Illustrative preparations of the glucosyltransferase of the present invention include oral preparations for the prevention of dental caries, such as tooth pastes, mouth washes and troches; and preparations suitable for addition to foods, beverages and drinks, e.g., sweetenings such as sugar, Castilla (sponge-cake-like product containing additional sweetening and a different texture), soft bean jelly, sponge cake, butter cake, Bavarian cream, custard cream, butter cream, custard pudding, cookies, jams, lactic acid bacteria beverages, carbonated beverages, coffee drinks, coffee jelly, caramels, ice cream, chewing gum, juices, candies and chocolate. Upon production of these oral preparations, foods, beverages and drinks, commonly-used, suitable ingredients can also be used in combination as needed. Examples of additives for oral preparations include calcium carbonate, calcium hydrogenphosphate, silica, magnesium carbonate, glycerin, sorbitol, propylene glycol, polyethylene glycol, carboxymethylcellulose, methylcellulose, sodium alginate, carageenan, carboxylvinyl polymer, sodium dioctylsulfosuccinate, sodium laurylsulfate, sodium dodecylbenzenesulfonate, butyl paraoxybenzoate, hinokitiol, allantoin, glytylricin, alcohol, gum arabic, starch, corn starch, saccharin sodium, stevioside, glucose, lactose, magnesium stearate, monopotassium phosphate, dipotassium phosphate, menthol, eucalyptus oil, peppermint, spearmint, and pigments. In addition, fluorides such as sodium fluoride and sodium monofluorophosphate; antiinflammatory agents such as lysozyme chloride and azulene; sodium chloride; and the like can also be added as needed.

On the other hand, beverages and drinks can be produced by adding those routinely employed as raw materials for beverages and drinks as needed, including, for example, glucose, fructose, sucrose, maltose, sorbitol, stevioside, corn syrup, lactose, citric acid, tartric acid, malic acid, succinic acid, lactic acid, L-ascorbic acid, dl-α-tocopherol, sodium erysorbate, glycerin, propylene glycol, glycerin fatty acid esters, polyglycerin fatty acid esters, sucrose fatty acid esters, sorbitan fatty acid esters, propylene glycol fatty acid esters, gum arabic, carageenan, casein, gelatin, pectin, agar, vitamin Bs, nicotinamide, calcium panthothenate, amino acids, calcium salts, pigments, essences, preservatives, etc.

For the production of anticarious foods, beverages and drinks - such as those described in subsequent examples - by adding the glucosyltransferase inhibitor of the present invention to foods, beverages and drinks, the glucosyltransferase inhibitor can be added in combination with sugar. In such cases, it is possible to add, in place of the glucosyltransferase and sugar, such anticarious sugars as illustrated in Examples 9-11 to be described subsequently.

Tea has been widely taken for many years throughout the world. Its extract and the non-adsorbed fraction which is obtained from the extract do not therefore present any question of safety. It is however preferred to control the content of the active ingredient in the glucosyltransferase inhibitor of the present invention within the range of 0.0001-10% in terms of dry weight from the standpoints of the effects of the glucosyltransferase inhibition activity and the taste, flavor, color tone and the like when the glucosyltransferase inhibitor is added.

The present invention will hereinafter be described in further detail by the following examples of the preparation methods of the extract of fermented tea leaves and the non-adsorbed fraction, a glucosyltransferase inhibition activity test and the preparation of oral sanitizers.

Example 1 (Preparation of extract)

Oolong tea leaves (100 g) was placed in a 2,000-mℓ Erlenmeyer flask, followed by the addition of 1,000 mℓ of hot water. The flask was heated at 90 °C for 15 minutes over a water bath to conduct extraction. The extract was filtered through "Celite" (trade mark), and the filtrate thus obtained was lyophilized to obtain 16.5 g of an extract.

The above procedures were repeated in respect of black tea leaves and Pu-erh tea leaves, whereby extracts were obtained in amounts of 16.4 g and 17.4 g, respectively.

Example 2 (Preparation of extract)

Oolong tea leaves (100 g) was placed in a 2,000-mℓ Erlenmeyer flask, followed by the addition of 1,000 mℓ of 50 vol.% ethanol. At room temperature, the tea leaves were extracted for 3 hours with gentle stirring every hour. The extract was filtered through "Celite" (trade mark), and the filtrate thus obtained was concentrated under reduced pressure to remove ethanol. Water was added to the residue, followed by lyophilization to obtain 29.2 g of an extract.

The above procedures were repeated in respect of black tea leaves and Pu-erh tea leaves, whereby extracts were obtained in amounts of 30.4 g and 31.3 g, respectively.

Example 3 (Preparation of non-adsorbed fraction)

Oolong tea extract (15 g) which had been obtained following the procedures of Example 1 was dissolved in 600 mℓ of water. The solution was charged into a column (4.4 x 20 cm) which was packed with "DIAION HP 21", whereby adsorption took place. A fraction not adsorbed on the adsorbent was combined with a washing obtained by washing the column with 2 ℓ of water after the adsorbing operation, whereby a non-adsorbed fraction was obtained. The non-adsorbed fraction was concentrated under reduced pressure and then lyophilized, whereby 6.4 g of a sample was obtained.

The above procedures were repeated in respect of black tea leaves and Pu-erh tea leaves, whereby non-adsorbed fractions were obtained in amounts of 7.7 g and 6.3 g, respectively.

Example 4 (Assay of glucosyltransferase inhibition activity)

(Enzyme solution)

As an enzyme solution, was used an extract which was obtained by culturing *S. mutans* MT8148 strain on Todd-Hewitt medium and then extracting hyphae with 8M urea in accordance with the method proposed by Hamada et al. [S. Hamada et al., J. Gen. Microbiol., **135**, 335-344 (1989)].

(Measuring method)

A reaction system was prepared by adding 0.15 mℓ of an aqueous solution of a sample, said solution having been prepared to contain the sample at the concentration of 2,000 ppm, the enzyme solution prepared from the *S. mutans* strain and water to 0.6 mℓ of 500 mM sodium phosphate buffer which had pH 6.0 and contained 5% of sucrose, 0.5% of dextran T10 and 0.5% of sodium azide. The water was added in an amount to give a total volume of 3 mℓ. They were reacted in a glass test tube. In the above measurement, the amount of the enzyme was set such that the absorbance at 550 nm became about 1.0 when reacted at 37 °C for 3 hours.

Resultant insoluble glucan was subjected to ultrasonic disintegration and the absorbance (A) at 550 nm was measured. Using as control (B) the absorbance obtained from the use of water in place of the sample solution, the inhibition rate (%) was determined in accordance with the following calculation formula:

$$\text{Inhibition rate (\%)} = \frac{100 \times (B - A)}{B}$$

(Measurement results)

The glucosyltransferase inhibition activities of the extracts of the various fermented tea leaves, said extracts having been obtained in Examples 1, 2 and 3, and of caffeine and catechins, which are representative components of tea leaves, were measured using the above reaction system. The results are summarized in Table 1.

Table 1

Sample tested	Inhibition rate, %
Oolong tea extract of Example 1	51
Black tea extract of Example 1	87
Pu-erh tea extract of Example 1	72
Oolong tea extract of Example 2	59
Black tea extract of Example 2	89
Pu-erh tea extract of Example 2	75
Non-adsorbed fraction of Oolong tea extract of Example 3	81
Non-adsorbed fraction of black tea extract of Example 3	94
Non-adsorbed fraction of Pu-erh tea extract of Example 3	76
Gallocatechin	15
Epigallocatechin	11
Catechin	13
Epicatechin	14
Epicatechin gallate	19
Epigallocatechin gallate	17

Example 5 (Tooth paste)

(Composition)	(Parts by weight)
Calcium hydrogenphosphate	42
Glycerin	18
Carageenan	0.9
Sodium laurylsulfate	1.2
Saccharin sodium	0.09
Butyl paraoxybenzoate	0.005
Extract of fermented tea leaves*	0.05
Perfume	1
Water	Balance
TOTAL	100

* Oolong tea extract obtained in Example 1.

Example 6 (Mouth wash)

(Composition)	(Parts by weight)
Sodium laurylsulfate	0.8
Glycerin	7
Sorbitol	5
Ethyl alcohol	15
Extract of fermented tea leaves*	0.05
l-Menthol	0.05
Perfume	0.04
Saccharin sodium	0.1
Water	Balance
TOTAL	100

* Black tea extract obtained in Example 1.

Example 7 (Troches)

(Composition)	(Parts by weight)
Gum arabic	6
Glucose	73
Extract of fermented tea leaves*	0.02
Potassium dihydrogenphosphate	0.2
Dipotassium hydrogenphosphate	0.1
Lactose	17
Essence	0.1
Magnesium stearate	Balance
TOTAL	100

* Pu-erh tea extract obtained in Example 2.

Example 8 (Preparation of anticarious sugar (powder))

(Procedures)

A liquid mixture of the below-described composition was heated at 80-90°C to dissolve the solid ingredients. The resultant solution was transferred to a rectangular stainless vat and then caused to dry up in a dryer controlled at 105°C. During the drying, the solution was mixed every hour. After the drying, the resultant solid was ground to convert it into the form of a powder sugar.

(Composition)	(Parts by weight)
Sugar	200
Extract of fermented tea leaves*	1
Water	30

*As the extract of fermented tea leaves, any one of Oolong tea extract, black tea extract and Pu-erh tear extract, which were obtained in Examples 1-3, is usable.

Example 9 (Preparation of anticarious sugar (powder))

(Procedures)

Using the below-described composition, sugar according to the present invention was spray granulated in a spray granulation apparatus ("Flow Coater Multi TLO-5M", trade name; manufactured by Okawa Mfg. Co., Ltd., Tokyo, Japan). Namely, sugar was placed in a batch container and then pre-dried at the hot air

temperature of 90°C for about 2 hours. Fermented tea extract which had been dissolved in water was sprayed against the sugar at the rate of 100 ml/min for 30 seconds by a spray gun. The spraying was then stopped and intermediate drying was conducted for 20 minutes. Spraying and intermediate drying were repeated 4 times, followed by finish drying for 20 minutes. The resultant sugar was cooled for 20 minutes, whereby an anticarious sugar was obtained.

(Composition)	(Parts by weight)
Sugar	200
Extract of fermented tea leaves*	1
Water	10

*As the extract of fermented tea leaves, any one of Oolong tea extract, black tea extract and Pu-erh tear extract, which were obtained in Examples 1-3, is usable.

Example 10 (preparation of anticarious sugar (syrup))

(Procedures)

An extract (0.75 part) of fermented tea leaves was added to 50 parts of hot water, so that the former was dissolved. Sugar (150 parts) was added to the solution, whereby an anticarious sugar (syrup) according to the present invention was obtained.

As the extract of fermented tea leaves, any one of Oolong tea extract, black tea extract and Pu-erh tear extract, which were obtained in Examples 1 and 2, is usable.

Example 11 (Comparison of the sweetness of anticarious sugar)

An anticarious sugar according to the present invention was compared in sweetness with sugar and palatinose by organoleptic evaluation as will be described next.

(Test samples)

Anticarious sugar of the present invention:
The anticarious sugar obtained in Example 8 by using the Oolong tea extract of Example 1.
Sugar: Refined sugar (prime grade)
Palatinose: Crystalline palatinose

(Evaluation methods)

A 5% sugar solution was prepared as a control.

Using the anticarious sugar, 3%, 4%, 5%, 6% and 7% solutions were prepared. In addition, 6%, 8%, 10%, 12% and 14% solutions were also prepared from the palatinose. These solutions were subjected at room temperature to organoleptic evaluation by 10 panelists in accordance with the pair testing method. The anticarious sugar solution and palatinose solution, which were comparable in sweetness with the 5% sugar solution, were determined.

The results are summarized in Table 2.

Table 2

Sample	Sweetness
Sugar	1.0
Anticarious sugar	1.0
Palatinose	0.4

It is envisaged from the above results that the anticarious sugar of the present invention exhibits substantially the same degree of sweetness as sugar but palatinose, an anticarious sugar substitute, shows sweetness as low as less than half of sugar.

Example 12 (Solubility of anticarious sweetening)

The readiness of dissolution of sugar, an anticarious sugar and palatinose in water were compared in terms of solubility in the following manner.

(Test samples)

Anticarious sugar of the present invention:
The anticarious sugar obtained in Example 8 by using the Oolong tea extract of Example 1.
Sugar: Refined sugar (prime grade)
Palatinose: Crystalline palatinose

(Evaluation methods)

At 10°C, 30°C, 50°C and 70°C, the sugar, anticarious sugar and palatinose were independently added to distilled water as much as they were dissolved completely. Their temperature-dependent solubilities are shown in Table 3.

Table 3

Sample	Temperature			
	10°C	30°C	50°C	70°C
Sugar	63	68	72	74
Anticarious sugar	63	68	72	74
Palatinose	21	32	44	58

Solubility (g-solid/100 g-solution)

As is apparent from the foregoing results, the anticarious sugar according to the present invention shows the same solubility as sugar. In contrast, palatinose which is a typical anticarious sugar substitute has low solubility especially at low temperatures. It is therefore evident that the anticarious sugar according

to the present invention is easier to use compared with palatinose.

Example 13 (Anti-glucan formation test)

With respect to three samples consisting of sugar (refined sugar, prime grade), an anticarious sugar (Example 8) and palatinose (crystalline palatinose), the amounts of glucan independently produced by them were compared in the following manner. To a mixture consisting of 0.3 mℓ of a 10% sample solution, 0.3 mℓ of 1 M sodium phosphate buffer - which had pH 6.0 and contained 1.0% of dextran T10 and 1.0% of sodium azide - and a glucosyltransferase enzyme solution, water was added in an amount to give a total volume of 3 mℓ so that a reaction system was prepared. They were reacted in a glass test tube. In the above test, the amount of the enzyme was set such that the absorbance at 550 nm became about 1.0 when the sugar (refined sugar, prime grade) was reacted at 37 °C for 3 hours.

Insoluble glucan thus formed was subjected to ultrasonic disintegration, and the absorbance (A) at 550 nm was measured. Using as control (B) the absorbance achieved when the sugar was employed as a test sample, the relative amount (%) of the so-formed glucan to the sugar was determined in accordance with the below-described calculation formula. The results are given in Table 4.

As the glucosyltransferase enzyme solution, was used an extract which was obtained by culturing *S. mutans* MT8148 strain on Todd-Hewitt medium and then extracting hyphae with 8M urea in accordance with the method proposed by Hamada et al. [S. Hamada et al., J. Gen. Microbiol., **135**, 335-344 (1989)].

(Results)

Table 4

Sample	Relative amount of formed glucan, %
Sugar	100
Anticarious sugar	6
Palatinose	2

As is clearly understood from the above results, the anticarious sugar of the present invention tends to form much less glucan compared with sugar and has glucan-formation inhibitory activity close to palatinose, although it contains sugar as its principal ingredient.

Example 14 (Anti-plaque test)

With respect to sugar (refined sugar, prime grade), an anticarious sugar (which had been obtained in Example 10 using the Oolong tea extract) and palatinose (crystalline palatinose), an *in vitro* plaque formation test was conducted. The test was carried out in the following manner. Culture media were prepared by adding the test samples at the concentration of 5% to Dulbecco's modified Eagle's medium, respectively. 6-mℓ Portions of the media were added to glass test tubes, respectively, to which *S. mutans* MT8148 strain was planted. After the cells were cultured at 37 °C for 1 day under anaerobic conditions, the amounts of plaque adhered on the walls of the respective test tubes were weighed. The results are summarized in Table 5.

Table 5

Sample	Amount of plaque formed, mg
Sugar	25.62 ± 1.78*
Anticarious sugar	3.21 ± 0.54*
Palatinose	2.01 ± 0.22*

* Average ± S.D.

Example 15 (Chewing gum)

(Composition)	(Parts by weight)
Gum base	20
Calcium carbonate	2
Steviosite	0.1
Extract of fermented tea leaves*	0.01
Lactose	76.89
Essence	1
TOTAL	100

* Oolong tea extract obtained in Example 3.

Example 16 (Juice)

(Composition)	(Parts by weight)
Condensed frozen tangerine juice	5
Liquid sugar (fructose, glucose)	11
Citric acid	0.2
L-Ascorbic acid	0.02
Non-adsorbed fraction*	0.01
Essence	0.2
Color	0.1
Water	Balance
TOTAL	100

* Non-adsorbed fraction of the black tea extract obtained in Example 3.

Example 17 (Candies)

(Composition)	(Parts by weight)
Sorbitol powder	99.745
Essence	0.2
Non-adsorbed fraction*	0.005
Sorbitol seeds	0.05
TOTAL	100

* Non-adsorbed fraction of the Pu-erh tea extract obtained in Example 3.

Example 18 (Cookies):

Composition	Parts by Weight			
	Control	Composition 1	Composition 2	Composition 3
Soft wheat flour	31.9	31.77	31.77	31.77
Whole egg	16.0	16.0	16.0	16.0
Margarine	19.2	19.2	19.2	19.2
Refined sugar (prime grade)	25.5	25.5	25.5	25.5
Baking powder	0.2	0.2	0.2	0.2
Water	7.2	7.2	7.2	7.2
Oolong tea extract*		0.13		
Black tea extract**			0.13	
Pu-erh tea extract***				0.13
Total	100.0	100.0	100.0	100.0

* Any one of the oolong tea extracts obtained in Examples 1-3 is usable. This applies equally to the subsequent examples with the proviso that the proportion may be reduced to one tenth the value given in the table when the extract fraction obtained in Example 3 is used.

** Any one of the black tea extracts obtained in Examples 1-3 is usable. This applies equally to the subsequent examples with the proviso that the proportion may be reduced to one tenth the value given in the table when the extract fraction obtained in Example 3 is used.

*** Any one of the Pu-erh tea extracts obtained in Examples 1-3 is usable. This applies equally to the subsequent examples with the proviso that the proportion may be reduced to one tenth the value given in the table when the extract fraction obtained in Example 3 is used.

Example 19 (Jam):

Composition	Parts by Weight			
	Control	Composition 1	Composition 2	Composition 3
Strawberries	54.8	54.69	54.69	54.69
Granulated sugar	42.0	42.0	42.0	42.0
Citric acid	0.6	0.6	0.6	0.6
Pectin	2.4	2.4	2.4	2.4
Essence	0.1	0.1	0.1	0.1
Oolong tea extract		0.21		
Black tea extract			0.21	
Pu-erh tea extract				0.21
Total	100.0	100.0	100.0	100.0

Example 20 (Lactic Acid Bacteria Beverage):

Composition	Parts by Weight			
	Control	Composition 1	Composition 2	Composition 3
Fermented milk (milk solid: 21%)	14.76	14.76	14.76	14.76
Liquid sugar (fructose, glucose)	13.31	13.31	13.31	13.31
Pectin	0.5	0.5	0.5	0.5
Citric acid	0.08	0.08	0.08	0.08
Essence	0.15	0.15	0.15	0.15
Water	71.20	71.14	71.14	71.14
Oolong tea extract		0.06		
Black tea extract			0.06	
Pu-erh tea extract				0.06
Total	100.0	100.0	100.0	100.0

Example 21 (Carbonated Beverage):

Composition	Parts by Weight			
	Control	Composition 1	Composition 2	Composition 3
Granulated sugar	8.0	8.0	8.0	8.0
Condensed lemon juice	1.0	1.0	1.0	1.0
L-Ascorbic acid	0.10	0.10	0.10	0.10
Citric acid	0.06	0.06	0.06	0.06
Sodium citrate	0.05	0.05	0.05	0.05
Color	0.05	0.05	0.05	0.05
Essence	0.15	0.15	0.15	0.15
Carbonated water	90.59	90.55	90.55	90.55
Oolong tea extract		0.04		
Black tea extract			0.04	
Pu-erh tea extract				0.04
Total	100.0	100.0	100.0	100.0

Example 22 (Coffee Drink):

Composition	Parts by Weight			
	Control	Composition 1	Composition 2	Composition 3
Granulated sugar	8.0	8.0	8.0	8.0
Skim milk powder	5.0	5.0	5.0	5.0
Caramel	0.2	0.2	0.2	0.2
Coffee extract	2.0	2.0	2.0	2.0
Essence	0.1	0.1	0.1	0.1
Polyglycerine	0.05	0.05	0.05	0.05
Fatty acid ester				
Salt	0.05	0.05	0.05	0.05
Water	84.6	84.56	84.56	84.56
Oolong tea extract		0.04		
Black tea extract			0.04	
Pu-erh tea extract				0.04
Total	100.0	100.0	100.0	100.0

Example 23 (Ice Cream):

Composition	Parts by Weight			
	Control	Composition 1	Composition 2	Composition 3
Fresh cream (45% fat)	33.8	33.8	33.8	33.8
Skim milk powder	11.0	11.0	11.0	11.0
Granulated sugar	14.8	14.8	14.8	14.8
Sugar-added yolk	0.3	0.3	0.3	0.3
Vanilla essence	0.1	0.1	0.1	0.1
Water	40.0	39.93	39.93	39.93
Oolong tea extract		0.07		
Black tea extract			0.07	
Pu-erh tea extract				0.07
Total	100.0	100.0	100.0	100.0

Example 24 (Chocolate):

Composition	Parts by Weight			
	Control	Composition 1	Composition 2	Composition 3
Cocoa mass	18.0	18.0	18.0	18.0
Cocoa butter	20.0	19.77	19.77	19.77
Milk powder	15.0	15.0	15.0	15.0
Sugar	46.5	46.5	46.5	46.5
Lecithin	0.5	0.5	0.5	0.5
Oolong tea extract		0.23		
Black tea extract			0.23	
Pu-erh tea extract				0.23
Total	100.0	100.0	100.0	100.0

Claims

Claims for the following Contracting States : AT, BE, CH, LI, DE, DK, FR, GB, IT, LU, NL, SE

1. A glucosyltransferase inhibitor comprising as an active ingredient a non-adsorbed fraction of an extract of fermented tea leaves, said non-adsorbed fraction having been obtained by subjecting the extract to adsorption treatment while using a synthetic adsorbent selected from adsorbents produced by polymerisation of styrene and divinylbenzene or by polymerisation of methacrylic acid and said non-adsorbed fraction being other than extract fractions adsorbed on the synthetic adsorbent.

2. An inhibitor of claim 1, wherein a non-adsorbed fraction of an extract of fermented tea leaves is a fraction, wherein catechins and caffeine have been eliminated by adsorption treatment of the fermented tea extract.

3. The inhibitor of any one of claims 1 or 2, wherein the fermented tea leaves are selected from Oolong tea, black tea and Pu-erh tea.

4. The inhibitor of any one of claims 1 or 2, wherein the extract has been extracted with an aqueous solution which contains 0-90 vol.% of ethanol.

5. The inhibitor of any one of claims 1-3, which is an oral sanitizer.

6. The inhibitor of any one of claims 1-3, which is an anticarious agent.

7. A food or beverage for the prevention of dental caries, comprising an effective amount of the inhibitor of any one of claims 1-3.

8. Use of the non-adsorbed fraction of an extract of fermented tea leaves according to any one of Claims 1 to 4 for the production of a glucosyltransferase inhibitor.

9. The use of claim 8, wherein the glucosyltransferase inhibitor is an oral sanitizer.

10. The use of claim 8, wherein the glucosyltransferase inhibitor is an anticarious agent.

Claims for the following Contracting States : ES, GR

1. A process for the preparation of a glucosyltransferase inhibitor, characterized in that it comprises: (a) subjecting to extraction process a starting material based on Oolong tea leaves, black tea leaves and fermented Pu-erh tea leaves, using water or mixtures of water and one or more polar solvents as solvent, on a ratio of solvent to fermented tea leaves of 2-1,000 times by weight, at a temperature within the range of from room temperature to the boiling point of the solvent used under normal pressure, for a period of time in the range from 10 minutes to 24 hours; (b) subjecting the thus obtained extract to an adsorption process, treating same with a synthetic adsorbent selected from adsorbents produced by polymerization of styrene and divinylbenzene or by polymerization of methacrylic acid, this adsorption process being carried out in a column packed with said adsorbent charging the extract of step (a) through the upper part and washing with water, so as to obtain the non-adsorbed fraction substantially exempt of catechins and caffeine which correspond to the aforesaid inhibitor.

2. A process according to Claim 1, wherein the extract has been extracted with an aqueous solution which contains 0-90 vol. % of ethanol.

3. A food or beverage, characterized by including the inhibitor obtained through the process of Claim 1, in an effective amount to provide preventive capacities against dental caries.

4. A process for obtaining a food or beverage for the prevention of dental caries, which comprises to add to said food or beverage an effective amount of the inhibitor obtained through the process of Claim 1.

Patentansprüche

Patentansprüche für folgende Vertragsstaaten : AT, BE, CH, LI, DE, DK, FR, GB, IT, LU, NL, SE

1. Glykosyltransferase-Inhibitor, der als aktiven Bestandteil eine nicht-adsorbierte Fraktion eines Extrakts von fermentierten Teeblättern umfaßt, wobei die nicht-adsorbierte Fraktion dadurch erhalten worden ist, daß man den Extrakt einer Adsorptionsbehandlung unter Verwendung eines synthetischen Adsorbens unterzieht, das aus Adsorbenzien ausgewählt ist, die durch Polymerisation von Styrol und Divinylbenzol oder durch Polymerisation von Methacrylsäure hergestellt worden sind, und wobei die nicht-adsorbierte Fraktion von den Extrakt-Fraktionen verschieden ist, die auf dem synthetischen Adsorbens adsorbiert werden.

2. Inhibitor nach Anspruch 1, in dem eine nicht-adsorbierte Fraktion eines Extrakts von fermentierten Teeblättern eine Fraktion ist, in der Katechine und Koffein durch Adsorptionsbehandlung des fermentierten Tee-Extrakts entfernt worden sind.

3. Inhibitor nach irgendeinem der Ansprüche 1 oder 2, in dem die fermentierten Teeblätter aus Oolong-Tee, schwarzem Tee und Pu-erh-Tee ausgewählt sind.

4. Inhibitor nach irgendeinem der Ansprüche 1 oder 2, in dem der Extrakt mit einer wäßrigen Lösung extrahiert worden ist, die 0 - 90 Vol.-% Ethanol enthält.

5. Inhibitor nach irgendeinem der Ansprüche 1 bis 3, der ein mundhygienisches Mittel ist.

6. Inhibitor nach irgendeinem der Ansprüche 1 bis 3, der ein Antikaries-Mittel ist.

7. Nahrungsmittel oder Getränk zur Verhütung von Zahnkaries, umfassend eine wirksame Menge des Inhibitors nach irgendeinem der Ansprüche 1 bis 3.

8. Verwendung der nicht-adsorbierten Fraktion eines Extrakts von fermentierten Teeblättern nach irgendeinem der Ansprüche 1 bis 4 bei der Herstellung eines Glykosyltransferase-Inhibitors.

9. Verwendung nach Anspruch 8, in dem der Glykosyltransferase-Inhibitor ein mundhygienisches Mittel ist.

10. Verwendung nach Anspruch 8, in dem der Glykosyltransferase-Inhibitor ein Antikaries-Mittel ist.

Patentansprüche für folgende Vertragsstaaten : ES, GR

1. Verfahren zur Herstellung eines Glykosyltransferase-Inhibitors, dadurch gekennzeichnet, daß es umfaßt, daß man (a) ein Ausgangsmaterial auf der Basis von Oolong-Teeblättern, schwarzen Teeblättern und fermentierten Pu-erh-Teeblättern bei einer Temperatur im Bereich von Raumtemperatur bis zum Siedepunkt des verwendeten Lösungsmittels bei Normaldruck über einen Zeitraum im Bereich von 10 Minuten bis 24 Stunden einem Extraktionsverfahren unterzieht, wobei man Wasser oder Mischungen von Wasser und einem oder mehreren polaren Lösungsmitteln als Lösungsmittel in einem 2-1000fachen Verhältnis des Gewichts von Lösungsmittel zu fermentierten Teeblättern verwendet; (b) den so erhaltenen Extrakt einem Adsorptionsverfahren unterzieht, wobei man denselben mit einem synthetischen Adsorbens behandelt, das aus Adsorbenzien ausgewählt ist, die durch Polymerisation von Styrol und Divinylbenzol oder durch Polymerisation von Methacrylsäure hergestellt worden sind, wobei dieses Adsorptionsverfahren in einer Säule durchgeführt wird, die mit dem Adsorbens gepackt ist, wobei man den Extrakt von Schritt (a) durch den oberen Teil einfüllt und mit Wasser wäscht, um die nicht-adsorbierte Fraktion im wesentlichen frei von Katechinen und Koffein zu erhalten, welche dem genannten Inhibitor entspricht.

2. Verfahren nach Anspruch 1, in dem der Extrakt mit einer wäßrigen Lösung, die 0 - 90 Vol.-% Ethanol enthält, extrahiert worden ist.

3. Nahrungsmittel oder Getränk, dadurch gekennzeichnet, daß man den durch das Verfahren von Anspruch 1 erhaltenen Inhibitor in einer wirksamen Menge einschließt, um verhütende Eigenschaften für

Zahnkaries bereitzustellen.

4. Verfahren zum Erhalten eines Nahrungsmittels oder Getränks zur Verhütung von Zahnkaries, welches umfaßt, daß man dem Nahrungsmittel oder Getränk eine wirksame Menge des durch das Verfahren des Anspruchs 1 erhaltenen Inhibitors zusetzt.

Revendications

Revendications pour les Etats contractants suivants : AT, BE, CH, LI, DE, DK, FR, GB, IT, LU, NL, SE

1. Inhibiteur de la glucosyltransférase, comprenant comme ingrédient actif une fraction non adsorbée d'un extrait de feuilles de thé fermentées, ladite fraction non adsorbée ayant été obtenue en soumettant l'extrait à un traitement d'adsorption en recourant à un adsorbant de synthèse choisi parmi des adsorbants produits par polymérisation de styrène et de divinylbenzène ou par polymérisation d'acide méthacrylique, et ladite fraction non adsorbée étant différente des fractions d'extrait adsorbées sur l'adsorbant de synthèse.

2. Inhibiteur selon la revendication 1, dans lequel une fraction non adsorbée d'un extrait de feuilles de thé fermentées est une fraction dans laquelle les catéchines et la caféine ont été éliminées par un traitement d'adsorption de l'extrait de thé fermenté.

3. Inhibiteur selon l'une quelconque des revendications 1 et 2, dans lequel les feuilles de thé fermentées sont choisies parmi le thé Oolong, le thé noir et le thé Pu-erh.

4. Inhibiteur selon l'une quelconque des revendications 1 et 2, dans lequel l'extrait a été obtenu par extraction avec une solution aqueuse qui contient 0-90% en volume d'éthanol.

5. Inhibiteur selon l'une quelconque des revendications 1-3, qui est un produit d'hygiène buccale.

6. Inhibiteur selon l'une quelconque des revendications 1-3, qui est un agent anti-caries.

7. Aliment ou breuvage pour la prévention de caries dentaires, comprenant une quantité efficace de l'inhibiteur selon l'une quelconque des revendications 1-3.

8. Utilisation de la fraction non adsorbée d'un extrait de feuilles de thé fermentées selon l'une quelconque des revendications 1 à 4 pour la production d'un inhibiteur de la glucosyltransférase.

9. Utilisation selon la revendication 8, dans laquelle l'inhibiteur de la glucosyltransférase est un produit d'hygiène buccale.

10. Utilisation selon la revendication 8, dans laquelle l'inhibiteur de la glucosyltransférase est un agent anticaries.

Revendications pour les Etats contractants suivants : ES, GR

1. Procédé pour la préparation d'un inhibiteur de la glucosyltransférase, caractérisé en ce qu'il comprend les opérations consistant à (a) soumettre à une opération d'extraction un matériau de départ à base de feuilles de thé Oolong fermentées, de feuilles de thé noir fermentées et de feuilles de thé Pu-erh fermentées, en utilisant comme solvant de l'eau ou des mélanges d'eau et d'un ou de plusieurs solvants polaires, dans un rapport du solvant aux feuilles de thé fermentées de 2-1.000 fois en poids, à une température située dans la plage allant de la température ambiante au point d'ébullition du solvant utilisé sous pression normale, pendant une durée allant de 10 minutes à 24 heures; (b) soumettre l'extrait ainsi obtenu à une opération d'adsorption, traiter cet extrait avec un adsorbant de synthèse choisi parmi des adsorbants produits par polymérisation de styrène et de divinylbenzène ou par polymérisation d'acide méthacrylique, cette opération d'adsorption étant conduite dans une colonne remplie dudit adsorbant, en chargeant l'extrait de l'étape (a) par la partie supérieure et en lavant à l'eau, de manière à obtenir la fraction non adsorbée essentiellement exempte de catéchines et de caféine, et qui correspond audit inhibiteur.

2. Procédé selon la revendication 1, dans lequel l'extrait a été obtenu par extraction avec une solution aqueuse qui contient 0-90% en volume d'éthanol.

3. Aliment ou breuvage, caractérisé en ce qu'il comprend l'inhibiteur obtenu par le procédé de la revendication 1 dans une quantité efficace pour fournir des capacités de prévention contre les caries dentaires.

4. Procédé d'obtention d'un aliment ou d'un breuvage en vue de la prévention de caries dentaires, qui comporte l'opération consistant à ajouter audit aliment ou breuvage une quantité efficace de l'inhibiteur obtenu par le procédé de la revendication 1.